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ALKALOIDS FROM LEAVES AND ROOT BARK OF *ERVATAMIA HIRTA*

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Key Word Index—*Ervatamia hirta*; Apocynaceae; leaves; root bark; indole alkaloids; ^1H and ^{13}C NMR.

Abstract—During chemical investigation of the leaves and root bark of *Ervatamia hirta*, 33 alkaloids were isolated. Six are new: six are the 'monomeric' alkaloids (E) 16-*epi*-normacusine B, (E) 16-*epi*-affinisine, *O*-acetyl-16-*epi*-affinisine, affinisine-*N*(4)-oxide, dehydro-16-*epi*-affinisine, norfluorocurarine-*N*(4)-oxide, and the seventh is the indole 16-decarbomethoxyvoacamine-pseudoindoxyl. The known alkaloids are: (E) 16-*epi*-isositsirikine, β -yohimbine, 19,20-dehydro- β -yohimbine, β -yohimbine-pseudoindoxyl, isositsirikine, 19,20-dihydroisositsirikine, yohimbine-oxindole, normacusine B, affinisine, vobasine, dregamine, tabernaemontanine, norfluorocurarine, 12-hydroxynorfluorocurarine, apparicine, 3,14-dihydroellipticine, antirrhine, voacristine, ibogaine, iboxygaine, iboxygaine-hydroxyindolenine, iboluteine, 4',17,(17 β)-dihydrochibangensine, 16-decarbomethoxyvoacamine and 19,20-dihydro-16-decarbomethoxyvoacamine. Structural elucidation of the new alkaloids is based on spectral data and chemical correlations.

INTRODUCTION

As part of our continuing research on the genus *Ervatamia* [1, 2], we report our results on the alkaloid content of *E. hirta* [3, 4], which is a tree 5–7 m tall from Malaysia. The plant was included in the preparation of poisoned arrows and was used in traditional medicine for treatment of ulcerations of the nose [5]. Material was collected by T. Sévenet and J. R. Deverre at Trengganu (Malaysia). This work is a part of a collaborative research program between C.N.R.S. and the University of Malaya [6, 7].

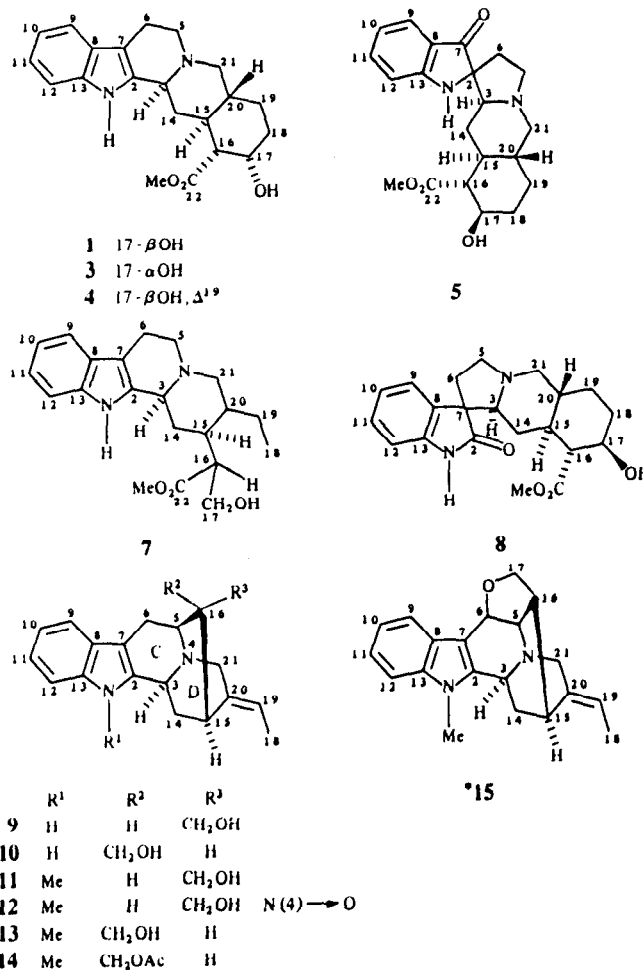
RESULTS AND DISCUSSION

Extractions were conducted in the usual fashion and the following alkaloid yields were obtained, 13.5 g kg⁻¹ (leaves) and 11.4 g kg⁻¹ (root bark). Direct crystallization from ethanol of the crude alkaloid mixture (AM) from the leaves afforded pure β -yohimbine (1) (69% AM). Five alkaloids were isolated from the resulting mother liquors (ML) by means of column and prep. TLC chromatography. They are (E) 16-*epi*-isositsirikine (2) (1.38% ML), β -yohimbine (3) (0.61% ML), 19,20-dehydro- β -yohimbine (4) (0.10% ML) and β -yohimbine-pseudoindoxyl (5) (0.09% ML). The root bark crude alkaloid mixture afforded together with 1 (29.6% AM), 2 (5.1% AM) and 3 (0.7% AM), 28 alkaloids: isositsirikine (6) (0.12% AM), 19,20-dihydroisositsirikine (7) (0.16% AM), β -yohimbine-oxindole (8) (0.02% AM), normacusine B (9) (0.70% AM), (E) 16-*epi*-normacusine B (10) (0.50% AM), affinisine (11) (0.21% AM), affinisine-*N*(4)-oxide (12) (0.13% AM), (E) 16-*epi*-affinisine (13) (3.4% AM), *O*-acetyl-16-*epi*-affinisine (14) (0.14% AM), dehydro-16-*epi*-affinisine (15) (0.16% AM), vobasine (16) (0.16% AM), dregamine (17) (0.10% AM), tabernaemontanine (18) (0.12% AM), nor-

fluorocurarine (19) (9.6% AM), norfluorocurarine-*N*(4)-oxide (20) (0.10% AM), 12-hydroxynorfluorocurarine (21) (1.76% AM), apparicine (22) (0.01% AM), 3,14-dihydroellipticine (23) (0.06% AM), antirrhine (24) (1.67% AM), voacristine (25) (0.05% AM), ibogaine (26) (2.17% AM), iboxygaine (27) (0.06% AM), iboxygaine-hydroxyindolenine (28) (0.04% AM), iboluteine (29) (0.22% AM), 4',17,(17 β)-dihydrochibangensine (30) (0.07% AM), 16-decarbomethoxyvoacamine (31) (3.23% AM), 19,20-dihydro-16-decarbomethoxyvoacamine (32) (0.21% AM) and 16-decarbomethoxyvoacamine-pseudoindoxyl (33) (0.30% AM).

Compounds 1, 3, 9, 11, 16–19, 22–25, 29 and 30 were identified by means of their spectral and co-TLC with reference samples. Alkaloids 2, 4–8, 21, 26–28, 31 and 32 were identified by comparison of their spectra with literature data. The novel isolation of 1, 3–5, 8, 19, 21, 23, 29 and 31 has provided the opportunity to obtain complete ^1H and ^{13}C NMR assignments (see Experimental) by means of 2D NMR experiments. The structures of the seven new alkaloids 10, 12–15, 20, 23 have been established by spectroscopic methods. Chemical correlations have confirmed the structure of alkaloids 12, 14, 15, 20.

The five new alkaloids 10, 12–15 possess a normacusine B-affinisine skeleton as shown by their ^1H NMR spectra [8], their UV spectra which display the three maxima of an indole chromophore, and their similar mass fragmentation (see Experimental). Compound 10 ($[\text{M}]^+$ at m/z 294) is a stereoisomer of normacusine B (9); compound 13 ($[\text{M}]^+$ at m/z 308) is a stereoisomer of affinisine 11; compound 12 ($[\text{M}]^+$ at m/z 324 and same fragments) is an *N*(4)-oxide derivative of 11 or of a stereoisomer; compound 14 which gives a $[\text{M}]^+$ at m/z 350 and an IR absorption at 1730 and 1240 cm⁻¹ is an *O*-acetyl derivative of 11 or of a stereoisomer; compound 15 ($[\text{M}]^+$ at m/z 306) is a dehydro derivative of 11.



* New alkaloids

Complete structures of these compounds were elucidated by ¹H and ¹³C NMR analysis.

Comparison of the chemical shift of H-5, H-6, H-14, H-16, H-17 of 10 and 13, respectively, with those of the corresponding protons of 9 and 11 indicates that the isomerism occurs at C-16 [8,9] and that 10 and 13 have the 16S configuration, assuming that they belong to the '15 α H' series. This is confirmed by the characteristic shielding of C-6, C-14 and C-17 of 10 and 13 compared to 9 and 11 [9,10]. The *E* geometry of the ethylidene side-chain of 10 and 13 is deduced from the observation of NOE between Me-18 and H-15. Additional proof is also provided by the chemical shifts of C-15 and C-21 of 9–11 and 13 that are consistent with an *E* geometry for the ethylidene side-chain [10]. Thus, 10 and 13 are 16-*epi*-normacusine B and 16-*epi*-affinisine, respectively. The geometry of the ethylidene group of koumidine, the *Z* isomer of 10, has recently been revised [9,11]. To the best of our knowledge, 10 has only been reported as a synthetic product [12].

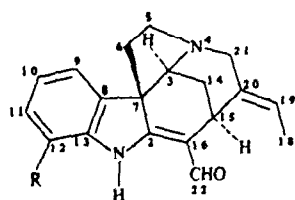
The parenthood of 14 with 16-*epi*-affinisine (13) is deduced from the similarity of their NMR spectral data (see Tables 1 and 2). The *O*-acetylation at C-17 is confirmed by the presence in the ¹H NMR spectrum of a three-proton singlet at δ 1.97, the downfield shift of the

methylene protons H-17 and the presence in the ¹³C NMR spectrum of the two carbons of the acetyl group (δ 20.9 and 170.4). The ¹³C resonances of carbons C-15 and C-21 (δ 26.6 and 56.3) establish the *E* configuration of the ethylidene side-chain [10]. Acetylation of 16-*epi*-affinisine (see Experimental) gave a compound identical (TLC, IR, mass spectrum, ¹H NMR) to 14.

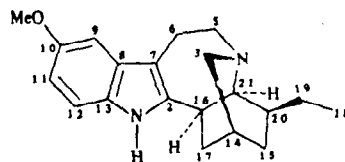
The structure of 12 has been elucidated after comparison of its NMR spectra with those of 11. In 12 the deshielding of the signals of H-3, H-5, the two methine carbons C-3, C-5, C-21 is characteristic of an *N*(4)-oxide derivative. This was demonstrated by conversion of 12 (see Experimental) into a compound identical (TLC, ¹H NMR) with 12.

Alkaloid 15 gave in its ¹H NMR spectrum a typical doublet for one proton ($J = 7.6$ Hz) at δ 5.6 assigned to the proton H-6 from 2D ¹H-¹H and ¹H-¹³C NMR experiments. Such a chemical shift is consistent with a hexacyclic structure related to a dehydrovoachalene type [13,14]. The deshielding of C-6 identified as a methine carbon (δ 71.4) and the chemical shifts of carbons C-5, C-17 and C-16 of 15 compared to those of 16-*epi*-affinisine (13) support the formation of a new bond between carbon C-6 and the oxygen atom located at C-17. The *E* geometry of the ethylidene side-chain

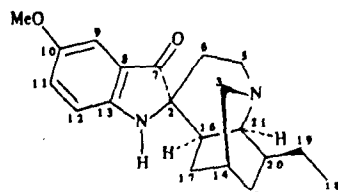
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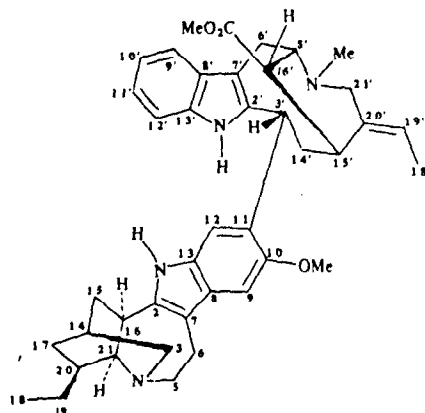
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 21 OH



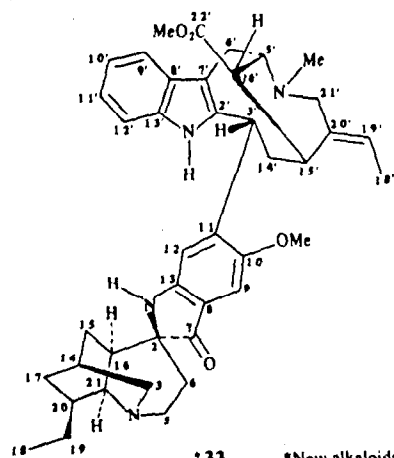
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*New alkaloids

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derived from the chemical shifts of C-15 and C-21 [10].
Synthesis of 15 was achieved by oxidation of 13 (see
Experimental).

Alkaloid 20 was identified from spectroscopic evidence.
UV spectrum was identical with that of norfluorocura-
rine (19) and the absorption band in the IR spectrum at
1660 cm⁻¹ characterises the conjugated C=O. Its mass
spectrum displayed a [M]⁺ at *m/z* 308 (16 mu more than
19). Compounds 19 and 20 also had an identical frag-
mentation (*m/z* 263, 249, 222, 208, 194, 180, 168, 121).
Comparison of ¹H and ¹³C NMR spectra of 19 and 20
indicates that 20 is the N(4)-oxide derivative of 19. In 20,
the protons and carbons in the neighbourhood of N(4)

were downfield shifted as in 12. Oxidation of norfluoro-
curarine 19 led to an identical compound (TLC, UV, IR,
mass spectrum, ¹H and ¹³C NMR) with 20.

The new bisindole alkaloid 33 (16-decarbomethoxy-
voacaminepseudoindoxyl) possesses in solution an
intense yellow-green fluorescent coloration which indic-
ates a pseudoindoxyl chromophore. This was confirmed
by the UV spectrum [absorptions at 228, 272 (sh), 294
(sh), 417 nm] and the absorption at 1660 cm⁻¹ in the IR
spectrum which displayed additional bands at 3360 cm⁻¹
(NH/OH) and 1720 cm⁻¹ (ester group). The mass spec-
trum of 33 showed a [M]⁺ at *m/z* 662 analysing for
C₄₁H₅₀N₄O₄ (16 mu more than 16-decarbomethoxy-

Table 1. ^{13}C NMR spectral data of alkaloids 10, 12–15 and 20 (75 MHz, CDCl_3 and int. ref. $\delta = 77$).

C	10	12	13	14	15	20
2	136.1	134.5	138.4	138.5	143.3	164.8
3	49.9	65.1	51.9	48.7	47.6	78.6
5	52.3	69.0	51.9	51.8	59.6	70.2
6	22.1	23.9	22.4	23.0	71.4	41.4
7	104.9	102.1	105.1	104.7	103.7	55.5
8	125.9	126.5	126.0	126.1	126.2	133.7*
9	117.7	118.6	118.1	118.1	118.9	121.5
10	118.7	119.1*	118.7	118.8	119.7	122.9
11	121.1	121.5	120.8	120.9	121.3	129.2
12	110.9	108.8	108.6	108.6	108.9	111.0
13	136.4	137.5	137.2	137.3	137.4	142.3
14	26.6	32.8	26.4	26.6	27.4	28.1
15	25.9	26.0	26.0	26.6	27.1	29.6
16	41.8	43.1	42.1	39.4	38.9	111.3
17	60.1	63.0	60.7	63.2	64.8	—
18	12.3	12.6	12.7	12.7	12.9	14.0
19	114.5	119.3*	113.4	113.9	114.0	127.0
20	138.0	130.6	139.0	139.0	138.9	134.4*
21	55.5	70.9	56.3	56.3	56.0	74.6
22	—	—	—	—	—	188.3
N(Me)-1	—	29.4	29.0	29.1	29.1	—
OAc	—	—	—	170.4	—	—
				20.9		

*Interchangeable values in a same column.

voacamine, 31) together with a low intensity peak at $[M + 14]^+$ as observed in 31 [15]. Fragments of the iboluteinyl moiety are present at m/z 108, 122, 124, 136, 138, 150, 176 [16] and those of the vobasiny moiety at m/z 122, 180, 182, 194 [17, 18]. The ^1H NMR spectrum of 33 was similar to that of 31 with the exception of the N-1 proton of the iboluteinyl part which was shielded upfield (Table 3) as expected for a pseudoindoxyl moiety. The ^{13}C NMR spectrum provides further evidence for this structure. Besides the carbons of the vobasiny moiety, characteristic carbons of the iboluteinyl moiety are observed: C-2 at $\delta 67.5$ and C-7 at $\delta 204.8$. The substitution at C-11 was confirmed by the chemical shift variations of the aromatic carbons of 33 compared with those of iboluteine 29. Identical variations occurred between 31 and ibogaine 26. The stereochemistry of C-3 is fixed for hindrance reasons as described previously [19].

In conclusion, *E. hirta* possesses a high alkaloidal content and a great variety of alkaloids which belong to types I and III [20]. Among the 33 isolated alkaloids, seven are new: 10, 12–15, 20 and 33. A striking feature of this plant is the presence of quasidimer (30) and yohimbine skeletons which are isolated for the first time from the genus *Ervatamia* [21, 22]. The large amount of β -yohimbine in the leaves (70% of AM) is in agreement with the pharmacological activity which has been observed in the course of preliminary study of this species.

EXPERIMENTAL

General. ^1H and ^{13}C NMR were recorded in CDCl_3 at 300 and 75 MHz, respectively. Chemical shifts are reported in δ from TMS. Prep. TLC as performed on silica gel K6F Whatman and

CC on silica gel 60 (70–230 mesh) Merck.

Plant material. *E. hirta* (Hook. f) King and Gamble was collected in September 1984 in Malaysia. A voucher specimen is kept at the herbarium of the Department of Phytocchemistry, University of Malaya under number D-235.

Extraction. Dried powdered leaves (0.6 kg) were wetted with 50% NH_4OH , macerated overnight in EtOAc, then triturated. The lixiviate was extracted with 2% H_2SO_4 . The aq. layer was basified with NH_4OH and extracted with CHCl_3 . The CHCl_3 layers were dried (Na_2SO_4) and evapd *in vacuo* to give 8.1 g of crude alkaloid mixture (AM). Extraction of root bark (3.3 kg) performed according to the same process gave 37.5 g of AM.

Isolation. Root bark AM was purified by CC on 2340 g silica gel packed in CHCl_3 ; 30 ml frs were collected. Elution was performed with CHCl_3 (3.9 l); CHCl_3 -MeOH (99:1, 7.5 l); (40:1, 9.6 l); (19:1, 9.6 l); (9:1, 7.05 l); (4:1, 7.35 l); (1:1, 7.2 l) and MeOH (9.48 l). Alkaloid 1 was in frs 695–820, 2 in frs 876–1040, 3 in frs 561–644, 6 in frs 846–875, 7 in frs 536–549, 8 in frs 821–834, 9 in frs 1161–1337, 10 in frs 1045–1160, 11 in frs 645–724, 12 in frs 645–670, 13 in frs 536–644, 14 in frs 421–430, 15 in frs 390–420, 16 in frs 421–457, 17 in frs 431–457, 18 in frs 321–380, 19 in frs 536–670, 20 in frs 561–644, 21 in frs 971–1080, 22 in frs 645–670, 23 in frs 681–1044, 24 in frs 1391–1500, 25 in frs 266–320, 27 and 28 in frs 536–549, 29 in frs 1601–2056, 30 in frs 1771–1900, 31 and 32 in frs 645–724, and 33 in frs 1700–2056.

Alkaloids from leaves were isolated and sep'd in a similar fashion. Alkaloid 1 was obtained by crystallization of crude AM from EtOH (yield 69%). The mother liquors of crystallization were purified by CC on 100 g silica gel packed in CHCl_3 ; 20 ml frs were collected. Elution was performed with CHCl_3 (1.3 l); CHCl_3 -MeOH, (99:1, 140 ml); (49:1, 360 ml); (24:1, 600 ml); (23:2, 880 ml); (4:1, 340 ml) and MeOH (580 ml). Alkaloid 1 was in frs 100–120, 2 in frs 134–164, 3 in frs 98–115, 4 in frs 100–164 and 5 in frs 118–149.

(E) 16-Epinormacusine B (10). Ceric sulphate TLC (CR) green then pale yellow: R_f 0.18 (CHCl_3 -MeOH, 9:1); $[\alpha]_D^{25} + 3^\circ$ (MeOH; c 0.25). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 226 (4.41), 281 (3.71), 290 (3.61 sh). IR $\nu_{\text{CHCl}_3} \text{cm}^{-1}$: 3220, 2920, 2840, 1450, 1310, 1280, 1160, 1020, 740. MS: m/z (rel. int.): 294 ($[M]^+$, 100), 293 (79), 279 (10), 277 (13), 263 (38), 249 (11), 195 (6), 182 (11), 169 (79), 164 (34), 156 (10), 144 (8), 130 (8); HRMS: $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}$ calcd 294.172, found 294.1709. ^1H and ^{13}C NMR see Tables 1 and 2.

Affinisine-N(4)-oxide (12). CR TLC grey-purple then yellow-orange: R_f 0.10 (CHCl_3 -MeOH, 9:1); $[\alpha]_D^{25} + 3^\circ$ (MeOH; c 0.25). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 226 (4.51), 284 (3.77), 292 (3.71 sh). IR $\nu_{\text{KBr}} \text{cm}^{-1}$: 3360, 2920, 1470, 1380, 1190, 1030, 740. MS: m/z (rel. int.): 324 ($[M]^+$, 100), 320 (100), 307 (100), 293 (42), 291 (23), 277 (79), 263 (23), 249 (17), 235 (15), 221 (19), 196 (11), 182 (59), 182 (40), 170 (23), 168 (19), 154 (8). ^1H and ^{13}C NMR see Tables 1 and 2. Hemisynthesis from affinisine (11). To a soln of affinisine (23 mg, 0.07 mmol) in CH_2Cl_2 (2 ml), 19 mg (1.5 mmol) *m*-chloroperbenzoic acid was added under magnetic stirring at 0° . After completion (TLC), the soln was cond in *vacuo*. The residue was purified by prep. TLC (CHCl_3 -MeOH, 9:1) and yielded affinisine-N(4)-oxide (12) (20 mg; yield 87%).

(E) 16-Epiaffinisine (13). CR TLC green then pale yellow: R_f 0.44 (CHCl_3 -MeOH, 9:1); $[\alpha]_D^{25} - 18^\circ$ (MeOH; c 0.25). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 229 (4.43), 286 (3.75), 293 (3.71 sh). IR $\nu_{\text{KBr}} \text{cm}^{-1}$: 3360, 2940, 1470, 1380, 1040, 750. MS: m/z (rel. int.): 308 ($[M]^+$, 100), 307 (58), 293 (8), 291 (10), 277 (33), 263 (11), 249 (8), 183 (65), 182 (54), 168 (21), 157 (8). HRMS: $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}$ calcd 308.1888, found 308.1867. ^1H and ^{13}C NMR see Tables 1 and 2.

O-Acetyl-16-epiaffinisine (14). CR TLC green then pale yellow: R_f 0.64 (CHCl_3 -MeOH, 9:1); $[\alpha]_D^{25} - 14^\circ$ (MeOH; c 0.5). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 228 (4.52), 285 (3.81), 292 (3.77 sh). IR

Table

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Table 2. ^1H NMR spectral data of alkaloids 10, 12–15, 20 (300 MHz, CDCl_3 , residual CHCl_3 used as int. ref. $\delta = 7.27$)

H	10*	12	13	14	15	20
3	4.04 <i>dd</i> (9.0; 4.3)	4.43 <i>br d</i> (10.0)	4.07 <i>dd</i> (10.3; 3.1)	4.20 <i>dd</i> (10.2; 3.2)	4.09 <i>dd</i> (9.8; 4.0)	4.49 <i>br s</i>
5	3.46–3.56 <i>m</i>	3.03 <i>br dd</i> (4.5; 7.0)	3.31–3.42 <i>m</i>	3.56–3.64 <i>m</i>	3.72–3.87 <i>m</i>	3.78–3.89 <i>m</i>
6	2.83–2.89 <i>m</i>	2.59 <i>d</i> (15.6)	2.75–2.84 <i>m</i>	2.91 <i>dd</i> (16.2; 1.1)	5.63 <i>d</i> (7.6)	4.04–4.18 <i>m</i> 2.51 <i>td</i> (13.0; 6.5)
9	7.35 <i>br d</i> (7.2)	7.29 <i>br d</i> (7.1)	7.40 <i>br d</i> (7.0)	7.48 <i>br d</i> (7.7)	7.72 <i>dd</i> (7.7; 1.2)	7.65 <i>br d</i> (7.2)
10	6.97 <i>td</i> (7.2; 1.0)	7.04 <i>br t</i> (7.1)	7.08 <i>td</i> (7.0; 1.2)	7.09 <i>td</i> (7.7; 1.2)	7.15 <i>td</i> (7.7; 1.2)	7.05 <i>td</i> (7.2; 1.1)
11	7.03 <i>td</i> (7.2; 1.0)	7.19 <i>br t</i> (7.1)	7.18 <i>td</i> (7.0; 1.2)	7.18 <i>td</i> (7.7; 1.2)	7.22 <i>td</i> (7.7; 1.2)	7.26 <i>td</i> (7.2; 1.1)
12	7.22 <i>br d</i> (7.2)	7.26 <i>br d</i> (7.1)	7.27 <i>br d</i> (7.0)	7.28 <i>br d</i> (7.7)	7.30 <i>dd</i> (7.7; 1.2)	6.95 <i>br d</i> (7.2)
14	1.69–1.84 <i>m</i>	1.62 <i>br d</i> (12.0)	1.59–1.67 <i>m</i>	1.80 <i>dt</i> (13.1; 3.5)	1.81–1.98 <i>m</i>	1.45 <i>dt</i> (14.5; 1.4)
	1.69–1.84 <i>m</i>	2.19 <i>br dd</i> (12.0; 10.0)	1.79 <i>br dd</i> (12.7; 10.3)	1.86–2.0 <i>m</i>	1.81–1.98 <i>m</i>	2.96 <i>ddd</i> (14.5; 4.0, 2.0)
15	2.81 <i>q</i> (3.0)	2.52 <i>br s</i>	2.75–2.84 <i>m</i>	2.79 <i>q</i> (3.5)	2.84 <i>q</i> (3.1)	3.78–3.89 <i>m</i>
16	2.03–2.15 <i>m</i>	1.87 <i>br q</i> (7.0)	1.97–2.09 <i>m</i>	2.25–2.36 <i>m</i>	2.24–2.36 <i>m</i>	—
17	3.07 <i>dd</i> (10.8; 8.9)	3.13–3.28 <i>m</i>	3.07 <i>dd</i> (10.6; 8.8)	3.75 <i>dd</i> (11.3–8.8)	3.43 <i>t</i> (9.5)	—
	3.39 <i>dd</i> (10.8–6.3)	3.13–3.28 <i>m</i>	3.36 <i>dd</i> (10.6; 6.6)	4.07 <i>dd</i> (13.3–6.7)	3.72–3.87 <i>m</i>	—
Me-18	1.55 <i>dt</i> (6.8; 1.9)	1.52 <i>br d</i> (6.7)	1.63 <i>dt</i> (6.8; 1.9)	1.65 <i>dt</i> (6.8; 2.0)	1.66 <i>dt</i> (6.8; 2.0)	1.67 <i>dt</i> (7.0; 1.0)
19	5.18 <i>br q</i> (6.8)	5.26 <i>br q</i> (6.7)	5.22 <i>br q</i> (6.8)	5.29 <i>qt</i> (6.8; 1.9)	5.33 <i>qt</i> (6.8; 2.0)	5.69 <i>qt</i> (7.0; 1.5)
21	3.46–3.56 <i>m</i>	3.88 <i>br d</i> (15.9)	3.56–3.62 <i>m</i>	3.68–3.73 <i>m</i>	3.72–3.87 <i>m</i>	4.04–4.18 <i>m</i>
	3.46–3.56 <i>m</i>	4.57 <i>br d</i> (15.9)	3.56–3.62 <i>m</i>	3.68–3.73 <i>m</i>	3.72–3.87 <i>m</i>	4.40 <i>br d</i> (14.0)
22	—	—	—	—	—	9.45 <i>s</i>
NH	9.45 <i>s</i>	—	—	—	—	10.22 <i>br s</i>
NMe	—	3.53 <i>s</i>	3.55 <i>s</i>	3.61 <i>s</i>	3.63 <i>s</i>	—
OAc	—	—	—	1.97 <i>s</i>	—	—

*Methanol- d_4 was added to favour solubilization.

IR $\nu_{\text{max}}^{\text{MeOH}}$: 2920, 1730, 1460, 1240, 740. MS: m/z (rel. int.): 350 (100), 349 (57), 291 (94), 277 (17), 263 (8), 249 (4), 209 (6), 196 (13) (100), 182 (61), 168 (21), 157 (10), 154 (6); HRMS.: $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_2$ calcd 350.1994, found 350.1997. ^1H and ^{13}C NMR see Tables 1 and 2. **Hemisynthesis of 14 from (E)16-epiaffinisine** (13). A soln of 13 (20 mg, 0.06 mmol) in CH_2Cl_2 (10 ml), 2 ml H_2O and a catalytic amount of 4-dimethylaminopyridine were added. The soln was stirred overnight then washed with Na_2SO_4 soln, satd NaHCO_3 soln and H_2O . The organic phase was dried (Na_2SO_4) and evapd to dryness. *O*-Acetylpiaffinisine (14) was purified by prep. TLC (Et_2O – MeOH , 1:1) yield 43%.

Hemisynthesis of 15 from (E)16-epiaffinisine (13). CR TLC violet, centre yellow: CHCl_3 – MeOH , 9:1. $[\alpha]_D^{25}$: +58.8° (MeOH ; c 0.25).

UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 224 (4.37), 281 (3.65), 290 (3.58 sh). IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 2920, 2860, 1460, 1080, 1040, 990, 740. MS: m/z (rel. int.): 306 ($[\text{M}]^+$, 100), 305 (25), 291 (10), 289 (15), 277 (10), 275 (11), 249 (6), 196 (25), 183 (61), 182 (79), 168 (8); HRMS.: $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}$ calcd 306.1732, found 306.1718. ^1H and ^{13}C NMR see Tables 1 and 2. **Hemisynthesis of 15 from (E)16-epiaffinisine** (13). To a soln of 13 (40 mg, 0.13 mmol) in THF (3 ml), 59 mg of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone were added. After 1 hr reflux, the soln was concd *in vacuo*. The residue dissolved in CH_2Cl_2 was washed (satd NaHCO_3 soln), the organic phase dried (Na_2SO_4) and concd *in vacuo*, yielding 15 in 97% yield.

Norfluorourarine-N(4)-oxide (20). CR TLC green then yellow: R_f : 0.17 (CHCl_3 – MeOH , 22:3). $[\alpha]_D^{25}$: –690° (MeOH ; c 1). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 203 (4.30), 241 (3.92), 299 (3.53), 361 (4.13).

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In our continuing study of the plants, we have isolated a new alkaloid, *flavescens*. This alkaloid was used as a *flavescens* [1, 2]. So far, it has been used as a *flavescens* and the isolation of the alkaloid, (–)-1, was reported.

Separations by TLC and preparation of the dry roots of *flavescens* (1), *flavescens* (2), *flavescens* (4), (–)-1, 5, 6-dehydrated *flavescens* (9) (1).